AMENDMENTS TO THE SPECIFICATION:

On page 1, after the title, please insert the following new paragraph as follows:

This application is a National Stage Application of PCT/JP2005/005918, filed March 29, 2005.

Please amend paragraph [0104] as follows:

[0104] A well known two-hybrid method can also be used for an identification method of the present invention. For example, the method can be carried out wherein a plasmid for expressing a fusion protein of the protein according to the present invention and a DNA binding protein, a plasmid for expressing a fusion protein of a Rho family protein and a transcription activating protein, and a plasmid containing a reporter gene that is linked to a suitable promoter gene are introduced to a yeast, a eukaryotic cell, or the like. The identification of a compound that inhibits the binding of the present protein to a Rho family protein can be achieved by comparing the amount of expression of the reporter gene, in the presence of a test compound, with an amount of expression of the reporter gene in the absence of the test compound. In the case that the amount of expression of the reporter gene in the presence of the test compound is decreased or eliminated, compared to the amount of expression of the reporter gene in the absence of the test compound, it can be determined that the test compound inhibits the binding function of the present protein to a Rho family protein. Any reporter genes that are used in a conventional reporter assay can be used herein. A reporter gene can be exemplified by a gene encoding a protein having an enzyme activity, such as, luciferase, β-Gal, chloramphenicol acetyl transferase, or the like. The expression of the reporter gene can be detected by determining the activity of the gene product, for example, an enzyme activity in the case of using the reporter gene exemplified

in the above.

Please amend paragraph [0111] as follows:

[0111] A method of identifying a compound that inhibits the expression of a polynucleotide according to the present invention can also be carried out by, for example, preparing a vector, that comprises a promoter region of a gene corresponding to the present polynucleotide and a reporter gene linked downstream of the promoter region instead of the present polynucleotide, and contacting a cell, e.g. a eukaryotic cell, which contains the vector, with the test compound, and then determining the presence or absence of, or a change in expression of the reporter gene. Any reporter genes that are used in a conventional reporter assay can be used herein. A reporter gene can be exemplified by a gene encoding a protein having an enzyme activity, such as, luciferase, β-Gal, chloramphenicol acetyl transferase, or the like. The expression of the reporter gene can be detected by determining the activity of the gene product, for example, an enzyme activity in the case of using a reporter gene exemplified above.

Please amend paragraph [0127] as follows:

[0127] The tissue distribution of the polynucleotide shown by the nucleotide sequence set forth in SEQ ID NO: 1, in the sequence listing, which is a specific example of a polynucleotide according to the present invention, was found to be approximately 5 times or more higher, specifically 4.5 times or more higher, in a stomach adenocarcinoid tumor, which is one of stomach tumors, as compared to that in a normal stomach tissue. The protein encoded by the polynucleotide shown by the nucleotide sequence set forth in SEQ ID NO: 1, has a DH/PH domain that is an active domain of Rho-GEF. Meanwhile, the polynucleotide (SEQ ID NO: 5),

also has a DH/PH domain coding region, which consists of the polynucleotide (SEQ ID NO: 3), shown by the nucleotide sequence from the 581st to the 1675th nucleotides of the nucleotide sequence set forth in SEQ ID NO: 1, and includes an oligonucleotide (SEQ ID NO: 19) ligated to its 5′-terminal. The oligonucleotide (SEQ ID NO: 19) consists of a kozak sequence and a methionine codon. When the polynucleotide (SEQ ID NO: 5) was co-expressed with a gene encoding a Rho family protein, in a mammalian cell, the product of the polynucleotide was bound to the Rho family protein, and the activation of the Rho family protein was accelerated. It can be considered from these findings that the protein encoded by the polynucleotide shown by the nucleotide sequence set forth in SEQ ID NO: 5, works as a Rho-GEF. The oligonucleotide (SEQ ID NO: 19) consisting of a kozak sequence and a methionine codon, which was added to the 5′-terminal of the polynucleotide shown by the nucleotide sequence set forth in SEQ ID NO: 3, does not significantly affect the function of the expressed protein. Therefore, the present inventors believe that the protein encoded by the polynucleotide shown by the nucleotide sequence set forth in SEQ ID NO: 3 also works as a Rho-GEF. Further, the nucleotide sequence set forth in SEQ ID NO: 1 contains the nucleotide sequence set forth in SEQ ID NO: 3. Therefore, the present inventors believe that the protein encoded by the polynucleotide shown by the nucleotide sequence set forth in SEQ ID NO: 1 also works as a Rho-GEF. Among the Rho-GEF genes isolated so far, vav (Non-Patent References 3 and 4), ost (Non-Patent Reference 5), ibc (Non-Patent Reference 6), and the like are known to relate to cancer. Thus, the present inventors believe that the high expression of the present polynucleotides relate to a stomach tumor. Therefore, the medicaments and the pharmaceutical compositions according to the present invention may be useful as agents for preventing and/or treating a stomach tumor. In addition, the medicaments and the pharmaceutical compositions may be used in methods of preventing and/or

treating a stomach tumor.

Please amend paragraph [0138] as follows:

[0138] Any known gene detection methods can be used for detecting a polynucleotide according to the present invention, or a gene containing the polynucleotide. Specifically, for example, plaque hybridization, colony hybridization, Southern blotting, Northern blotting, the NASBA method (nucleic acid sequence-based amplification method), reverse transcription-polymerase chain reaction (RT-PCR), or the like can be used. In addition, in situ RT-PCR, in situ hybridization, or the like, which allows cell level measurement, can be used for the detection. In such a gene detection method, it is useful to use an oligonucleotide, which consists of a partial sequence of a polynucleotide according to the present invention, and has the property as a probe or a primer, for carrying out the isolation and/or the amplification of the polynucleotide, a gene containing the polynucleotide, or a mutant gene thereof. The phrase "oligonucleotide having the property as a probe" means an oligonucleotide that is capable of specifically hybridizing only to a present polynucleotide, and consists of a characteristic sequence of a present polynucleotide. The phrase "oligonucleotide having the property as a primer" means an oligonucleotide that is capable of specifically amplifying only a present polynucleotide, and consists of a characteristic sequence of a present polynucleotide. Further, when detecting a mutant gene capable of being amplified, a primer or a probe having a sequence with a predetermined length, which contains a mutation site within the gene, is prepared and used. A probe and a primer may have a nucleotide sequence consisting of, preferably, from about 5 to 50 nucleotides, more preferably, from about 10 to 35 nucleotides, and even more preferably, from about 15 to 30 nucleotides. Specifically, an oligonucleotide shown by the nucleotide sequence set forth in SEQ ID NO: 7, SEQ ID NO: 8,

SEQ ID NO: 9, or SEQ ID NO: 10 can be preferably used as a primer for amplifying a polynucleotide of the present invention, or a fragment thereof, or as a probe for detecting a present polynucleotide. A labeled probe is normally used as the probe, but the unlabeled probe can also be used. Alternatively, the detection can also be carried out by measuring the specific binding to a ligand that was labeled directly or indirectly. Various methods are known for labeling a probe and a ligand. For example, nick translation, random priming, or a method utilizing kinase treatment, may be used. Labeling substances suitable for use include a radioactive isotope, biotin, a fluorescent substance, a chemiluminescent substance, an enzyme, an antibody, and the like.

Please amend paragraph [0140] as follows:

[0140] In addition to detection of a gene, PCR allows quantitative measurement of a polynucleotide according to the present invention, a gene containing the polynucleotide, or a mutant gene thereof. Such an assay method may be exemplified by a competitive assay, such as, an MSSA method (multi-channel simplex simulated annealing method), or PCR-SSCP (PCR-single strand conformation polymorphism), which is known as a mutation detection method that utilizes a change in mobility accompanying a structural change of a single-stranded DNA.

Please amend paragraph [0147] as follows:

[0147] The preferable methods of detecting a present protein or its mutant, may be, for example, enzyme-linked immunosorvent assay (ELISA), radio immuno assay (RIA), immunoradiometric assay (IRMA), and immunoenzymometric assay (IEMA), including a sandwich method using a monoclonal antibody and/or a polyclonal antibody. Alternatively, ~~radio~~

~~immuno-assay,~~ competitive binding assay, and the like may be employed.

Please amend paragraph [0179] as follows:

[0179] The hj03796 DH/PH (C-terminal FLAG-tagged protein) expression vector and the expression vector for expressing any one of the aforementioned Rho family proteins were transfected into 293EBNA cells that were plated in a 24 well plate. The transfection of cells with the vectors was carried out using a LipofectAMINE 2000. Cells which were not transfected with any vector, but were treated only with LipofectAMINE 2000, were used as a negative control. On the day after gene transfection, the cell was lysed with the lysis buffer containing a protease inhibitor cocktail of 1/100 concentration (SIGMA), to prepare a cell lysate. Then, the cell lysate was subjected to a reaction with effector ~~bed~~ beads (UPSTATE) at 4 °C, for 1 hour. The effector ~~bed~~ beads used herein ~~was~~ were glutathione agarose effector ~~bed~~ beads that ~~was~~ were conjugated with a GST-fusion protein prepared by adding a GST-tag to a binding domain of PAK-1, or Rhotekin, to the active the Rho family protein. After the reaction, the effector ~~bed~~ beads ~~was~~ were washed with the lysis buffer, and then subjected to extraction with extract solution (Tris/SDS/β-mercaptoethanol: Daiichi Pure Chemicals). The obtained extract was subjected to Western blotting using SDS-PAGE to carry out the detection of the FLAG-tagged protein using an anti-FLAG antibody. The lysis buffer was composed of 25 mM HEPES (pH 7.5), 150 mM NaCl, 10 mM $MgCl_2$, 1 mM EDTA, 2% glycerol, and 1% Triton X-100.

Please amend paragraph [0180] as follows:

[0180] If the hj03796 DH/PH had a GEF activity for a Rho family protein, the hj03796 DH/PH would induce conversion of the Rho family protein from an inactive form (GDP-bound

form) to an active form (GTP-bound form). PAK-1 that was used as effector ~~bed~~ beads is known to bind to both the active Cdc42 and the active Rac1. In addition, Rhotekin binds to the active RhoA. Therefore, if the hj03796 DH/PH had a GEF activity for a Rho family protein, the Rho family protein that binds to the effector ~~bed~~ beads would increase in amount. Then, it was decided that the hj03796 DH/PH had a GEF activity, when the band of the Rho family protein was detected by using an anti-FLAG antibody, more clearly in the sample prepared from the cells in which the hj03796 DH/PH was co-expressed with the Rho family proteins, than in the sample prepared from the cells in which only the Rho family proteins were expressed.